

WHAT IS CLAIMED IS:

1. An adhesion receptor comprising:
 - (a) an extracellular receptor domain,
 - wherein said extracellular receptor domain comprises a peptide that binds a target cell antigen;
 - wherein the target cell antigen is differentially expressed between healthy cells and target cells;
 - wherein the target cells are targeted for recognition and destruction by Natural Killer (NK) cells;
 - wherein the peptide that binds a target cell antigen comprises a monoclonal antibody, a polyclonal antibody, a recombinant antibody, a human antibody, a humanized antibody, a Fab, a Fab', a F(ab')₂, an Fv, a single-chain Fv (scFv), minibody, a diabody, and a single-domain antibody, a functional derivative thereof, a variant thereof or a fragment thereof; and
 - (b) a transmembrane domain, wherein the transmembrane domain anchors the extracellular receptor domain on the surface of the NK cell.
2. The adhesion receptor of claim 1, wherein the peptide that binds the target cell antigen is an antibody or an antibody fragment.
3. The adhesion receptor of claim 1 or 2, wherein the target cell antigen is associated with a neoplasm, cancer, or tumor.
4. An adhesion receptor according to any one of claims 1 to 3, wherein the target cell antigen is a tumor associated antigen.
5. An adhesion receptor according to any one of claims 1 to 3, wherein the target cell antigen is a tumor specific antigen.

6. An adhesion receptor according to any one of claims 1 to 4, wherein the target cell antigen comprises one or more of Fms-Like Tyrosine Kinase 3 (FLT3), Syndecan 1, epidermal growth factor receptor (EGFR), CD19, CD70, BCMA, Her2, PSMA, and CD123.

7. An adhesion receptor according to any one of claims 1 to 6, wherein the adhesion receptor comprises an anti-Her2 scFv, wherein the scFv comprises the amino acid sequence of SEQ ID NO: 59, SEQ ID NO: 61, or an amino acid sequence at least about 95% homologous to SEQ ID NO: 59 or SEQ ID NO: 61.

8. An adhesion receptor according to any one of claims 1 to 6, wherein the adhesion receptor comprises an anti-PSMA scFv, wherein the scFv comprises the amino acid sequence of SEQ ID NO: 63, SEQ ID NO: 65, or an amino acid sequence at least about 95% homologous to SEQ ID NO: 63 or SEQ ID NO: 65.

9. An adhesion receptor according to any one of claims 1 to 8, wherein the extracellular receptor domain further comprises a second peptide that binds a different target cell antigen than the first peptide or wherein the extracellular receptor domain further comprises a second peptide that binds the same target cell antigen as the first peptide.

10. A polynucleotide encoding the adhesion receptor according to any one of claims 1 to 9, wherein the polynucleotide is operably linked to at least one regulatory element for the expression of the adhesion receptor.

11. The polynucleotide of claim 10, wherein the polynucleotide further encodes membrane-bound interleukin 15 (mbIL15).

12. The polynucleotide of claim 11, wherein the mbIL15 is encoded by a sequence having at least about 95% homology to SEQ ID NO: 16.

13. The polynucleotide of any one of claims 10 to 12, wherein the polynucleotide encodes a second adhesion receptor, wherein the first and second adhesion receptors

bind different target cell antigens, wherein the first and second adhesion receptors bind the same target cell antigen, or wherein the first and second adhesion receptors bind different epitopes of the same target cell antigen.

14. A vector comprising a polynucleotide of any one of claims 10 to 13, wherein the polynucleotide is operatively linked to at least one regulatory element for expression of the adhesion receptor.

15. The vector of claim 14, wherein the vector further encodes a chimeric receptor comprising an extracellular receptor domain and an effector domain, wherein said extracellular receptor domain comprises a peptide that binds native ligands of Natural Killer Group 2 member D (NKG2D), and wherein said effector domain comprises a transmembrane region and an intracellular signaling domain.

16. The vector of claim 14 or 15, wherein the vector is a retrovirus.

17. A genetically engineered immune cell expressing the adhesion receptor according to any one of claims 1 to 9, comprising the polynucleotide according to any one of claims 10 to 13, or the vector according to any one of claims 14 to 16.

18. The genetically engineered immune cell of claim 17, wherein the genetically engineered immune cell comprises a natural killer (NK) cell.

19. The genetically engineered immune cell of claim 17 or 18, wherein the genetically engineered immune cell is an autologous cell isolated from a patient.

20. The genetically engineered immune cell of claim 17 or 18, wherein the genetically engineered immune cell is an allogeneic cell isolated from a donor.

21. A genetically engineered immune cell according to any one of claims 17 to 20, further comprising:

a chimeric receptor comprising:

(a) an extracellular receptor domain, wherein said extracellular receptor domain comprises a peptide that binds native ligands of Natural Killer Group 2 member D (NKG2D); and

(b) an effector domain comprising a transmembrane region and an intracellular signaling domain.

22. A genetically engineered NK cell, comprising:

(i) an adhesion receptor, comprising an extracellular receptor domain and a transmembrane domain,

wherein said extracellular receptor domain comprises a peptide that binds a target cell antigen,

wherein the target cell antigen is differentially expressed between healthy cells and target cells,

wherein the peptide that binds a target cell antigen comprises a monoclonal antibody, a polyclonal antibody, a recombinant antibody, a human antibody, a humanized antibody, a Fab, a Fab', a F(ab')₂, an Fv, a single-chain Fv (scFv), minibody, a diabody, and a single-domain antibody, a functional derivative thereof, a variant thereof or a fragment thereof, and

wherein the transmembrane domain anchors the extracellular receptor domain on the surface of the NK cell;

(ii) a chimeric receptor comprising an extracellular receptor domain and an effector domain,

wherein said extracellular receptor domain comprises a peptide that binds native ligands of Natural Killer Group 2 member D (NKG2D), and

wherein said effector domain comprises a transmembrane region and an intracellular signaling domain.

23. The genetically engineered NK cell of claim 22, wherein the cell further comprises, (c), membrane bound IL15 (mbIL15).

24. The genetically engineered NK cell of claim 22 or 23, wherein the target cell antigen comprises one or more of Fms-Like Tyrosine Kinase 3 (FLT3),

Syndecan 1, epidermal growth factor receptor (EGFR), CD19, CD70, BCMA, Her2, PSMA, and CD123, and wherein the mbIL15 comprises the amino acid sequence of SEQ ID NO: 17, or a sequence having at least about 95% homology thereto.

25. A genetically engineered NK cell according to any one of claims 22 to 24, wherein said NK cell is an allogeneic cell isolated from a donor.

26. An amino acid sequence of SEQ ID NO: 59, SEQ ID NO: 61, or an amino acid sequence at least about 95% homologous to SEQ ID NO: 59 or SEQ ID NO: 61.

27. An amino acid sequence of SEQ ID NO: 63, SEQ ID NO: 65, or an amino acid sequence at least about 95% homologous to SEQ ID NO: 63 or SEQ ID NO: 65.

28. A method for generating a genetically engineered NK cell with enhanced cytotoxicity, comprising:

contacting a population of NK cells with a vector encoding an adhesion receptor,

wherein the adhesion receptor comprises an extracellular receptor domain and a transmembrane domain,

wherein said extracellular receptor domain comprises a peptide that binds a target cell antigen,

wherein the target cell antigen is differentially expressed between healthy cells and target cells,

wherein the peptide that binds a target cell antigen comprises a monoclonal antibody, a polyclonal antibody, a recombinant antibody, a human antibody, a humanized antibody, a Fab, a Fab', a F(ab')₂, an Fv, a single-chain Fv (scFv), minibody, a diabody, and a single-domain antibody, a functional derivative thereof, a variant thereof or a fragment thereof, and

wherein the transmembrane domain anchors the extracellular receptor domain on the surface of the NK cell.

29. The method of claim 28, wherein the method further comprises contacting a population of NK cells with a vector encoding a chimeric receptor comprising an extracellular receptor domain and an effector domain, wherein said extracellular receptor domain comprises a peptide that binds native ligands of Natural Killer Group 2 member D (NKG2D), and wherein said effector domain comprises a transmembrane region and an intracellular signaling domain.

30. Use of the adhesion receptor according to any one of claims 1 to 9, the polynucleotide according to any one of claims 10 to 13, the vector according to any one of claims 14 to 16, the genetically engineered immune cell according to any one of claims 17 to 21, the genetically engineered NK cell according to any one of claims 22 to 25, the amino acid of claim 26 or 27, or the method according to any one of claims 28 to 29 for treating or preventing cancer in a mammal in need thereof.

31. Use of the adhesion receptor according to any one of claims 1 to 9, the polynucleotide according to any one of claims 10 to 13, the vector according to any one of claims 14 to 16, the genetically engineered immune cell according to any one of claims 17 to 21, the genetically engineered NK cell according to any one of claims 22 to 25, the amino acid of claim 26 or 27, or the method according to any one of claims 28 to 29 in the manufacture of a medicament for treating or preventing cancer in a mammal in need thereof.